Docket No. : 532552000101
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Paul TARDI, *et al.*

Serial No.: 10/417,631

Filing Date: April 16, 2003

For: COMPOSITIONS FOR DELIVERY OF DRUG COMBINATIONS

Confirmation No.: 6691

Group Art Unit: 1616

Examiner: Ali Soroush

DECLARATION OF LAWRENCE D. MAYER
UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Lawrence D. Mayer, declare as follows:

1. I am President and Head of Research of Celator Pharmaceuticals, Inc., the assignee herein. I have been actively engaged in drug delivery research, both academically and in industrial settings for over 22 years. A copy of my *curriculum vitae* is attached as Exhibit A.

2. I agree with the statement by the Examiner in his Office Action dated November 15, 2007, "...the state of the art is very high in terms of formulating the liposomal sustained release compositions..." Indeed there were numerous references in the art at the time

of the present application describing a wide range of approaches and methods for controlling the loading as well as release of liposomal agents with the latter being widely examined for a number of antineoplastic agents. Methods of modulating drug retention and release in multiple delivery vehicles, including liposomes and polymer-based nanoparticles, are well known to those of skill in the art. This literature includes an extensive compendium of data on actual release rates for a multiplicity of drugs from a multiplicity of particulate carriers.

3. Examples of methods for controlling liposomal drug release include:

a) the use of a transmembrane ion gradients, particularly pH gradients generated with, for example, citrate, ammonium sulfate or an ionophore as well as using various degrees of said pH gradients;

b) the use of transmembrane osmotic gradients of varying degrees;

c) modulating the class (*e.g.*, anionic, neutral, pegylated), acyl chain length and/or amount of individual phospholipids used in a mixture;

d) the addition of cholesterol;

e) altering the drug-to-lipid ratio;

f) selecting delivery vehicles with specific phase transition temperatures

4. Below is a list of references for each of the above categories. It should be noted that his list is only meant to provide representative methods and numerous other examples and related approaches were readily available:

a) Ionic Gradients

i. Cullis, P.R., *et al.*, Influence of pH gradients on the transbilayer transport of drugs, lipids, peptides and metal ions into large unilamellar vesicles. *Biochim. Biophys. Acta* (1997) 1331:187-211.

ii. Burke, T., and Gao, X., Stabilization of topotecan in low pH liposomes composed of distearoylphosphatidylcholine. *J. Pharm. Sciences* (1994) July; 83(7):967-969.

iii. Bowman, N., *et al.*, Liposomal vincristine which exhibits increased drug retention and increased circulation longevity cures mice bearing P388 tumors. *Cancer Res.* (1994) June 1; 54:2830:2833.

iv. Haran, G., *et al.*, Transmembrane ammonium sulfate gradients in liposomes produce efficient and stable entrapment of amphipathic weak bases. Biochim. *Biophys. Acta* (1993) Sept 19; 1151(2):201-215.

v. Fenske, D.B., *et al.*, Ionophore-mediated uptake of ciprofloxacin and vincristine into large unilamellar vesicles exhibiting transmembrane ion gradients. Biochim. *Biophys. Acta* (1998) Nov 11; 1414(1-2):188-204.

vi. Bowman, N., *et al.*, Optimization of the retention properties of vincristine in liposomal systems. *Biochim. Biophys. Acta* (1993) 1152:253-258.

vii. Clerc, S., and Barenholz, Y., Loading of amphipathic weak acids into liposomes in response to transmembrane calcium acetate gradients. *Biochim. Biophys. Acta* (1995) Dec 13; 1240(2):257-265.

viii. Redelmeier, T., *et al.*, Proton flux in large unilamellar vesicles in response to membrane potentials and pH gradients. *Biophys. J.* (1989) Aug; 56(2):385-393.

ix. US Patent 5,077,056 (Published December 31, 1991) – see Example 1 Part A – "Active Loading Using Na+ /K+ Gradients"

b) Osmotic Gradients

i. Mui, B.L., *et al.*, Influence of plasma on the osmotic sensitivity of large unilamellar vesicles prepared by extrusion. *J. Biol. Chem.* (1994) Mar 11;269(10).

ii. Allen, T.M., and Cleland, L.G., Serum-induced leakage of liposome contents. *Biochim. Biophys. Acta* (1980) 597:418-426.

c) **Lipid Composition**

i. Horowitz, A.T., *et al.*, *In vitro* cytotoxicity of liposome-encapsulated doxorubicin: dependence on liposome composition and drug release. *Biochim. Biophys. Acta* (1992) 1109:203-209.

ii. Frezard, F., and Garnier-Sullerot, A., Permeability of lipid bilayer to anthracycline derivatives. Role of the bilayer composition and of the temperature. *Biochim. Biophys. Acta* (1998) 1389:13-22.

iii. Lim, H.J., *et al.*, Role of drug release and liposome-mediated drug delivery in governing the therapeutic activity of liposomal mitoxantrone used to treat human A431 and LS180 solid tumors. *J. Pharmacol. Exp. Ther.* (2000) Jan;-292(1):337-345.

iv. Forssen, E.A., and Tokes, Z.A., Improved therapeutic benefits of doxorubicin by entrapment in anionic liposomes. *Cancer Res.* (1983) Feb; 43:546-550.

d) **Cholesterol Content**

i. Dos Santos, N., *et al.*, Improved retention of Idarubicin after intravenous injection obtained for cholesterol-free liposomes. *Biochim. Biophys. Acta* (2002) Jan; 1561:188-201.

ii. Ogihara-Umeda, I., and Kojima, S., Cholesterol enhances the delivery of liposome-encapsulated gallium-67 to tumors. *Eur. J. Nucl. Med.* (1989) 15:612-617.

iii. Fielding, R.M., and Abra, R.M., Factors affecting the release rate of terbutaline from liposome formulations after intratracheal instillation in the guinea pig. *Pharm. Res.* (1992) Feb; 9(2):220-223.

e) **Drug-to-Lipid Ratio**

i. Mayer, L., *et al.*, Influence of vesicle size, lipid composition, and drug-to-lipid ratio on the biological activity of liposomal doxorubicin in mice. *Cancer Res.* (1989) Nov. 1; 49:5922-5930.

f) **Phase Transition Temperature**

i. Hays, L.M., *et al.*, Factors affecting leakage of trapped solutes from phospholipid vesicles during thermotropic phase transitions. *Cryobiology* (2001) Mar; 42(2):88-102.

ii. Hayashi, H., *et al.*, Temperature-controlled release property of phospholipid vesicles bearing a thermo-sensitive polymer. *Biochim. Biophys. Acta* (1996) 1280:127-134.

iii. Anyarambhatla, G., and Needham, D., Enhancement of the phase transitions permeability of DPPC liposomes by incorporation of MPPC: A new temperature-sensitive liposome for use with mild hyperthermia. *J. Liposome Res.* (1999) 9(4):491-506.

iv. Kong, G., *et al.*, Efficacy of liposomes and hyperthermia in a human tumor xenograft model: Importance of triggered drug release. *Cancer Res.* (2000) Dec. 15; 60:6950-6957.

5. In addition, a similar database existed at the time of the invention describing methods for controlling drug release from natural and synthetic non-liposomal delivery vehicles including micelles, nanoparticles, microspheres and drug-polymer conjugates. Below is a list of references which detail various methods for controlling the release of therapeutic agents from non-liposomal delivery vehicles:

a) Genta, I., *et al.*, Different molecular weight chitosan microspheres: influence on drug loading and release. *Drug Dev. Ind. Pharm.* (1998) Aug; 24(8):779-784.

b) Kim, H., and Fassihi, R., Application of binary polymer system in drug release rate modulation. 2. Influence of formulation variables and hydrodynamic conditions on release kinetics. *J. Pharm. Sci.* (1997) Mar; 86(3):323-328.

c) Kawaguchi, T., *et al.*, Control of drug release with a combination of prodrug and polymer matrix: Antitumor activity and release profiles of 2',3'-Diacyl-5-fluoro-2'-deoxyuridine from Poly(3-hydroxybutyrate) microspheres. *J. Pharm. Sci.* (1992) June; 81(6):508-512.

d) Anderson, B.C., *et al.*, Understanding drug release from poly(ethylene oxide)-b-poly(propylene oxide)-b-poly(ethylene oxide) gels. *J. Control Release* (2001) Jan 29; 70(1-2):157-167.

e) Muller, R.H., *et al.*, Solid lipid nanoparticles (SLN) for controlled drug delivery – A review of the state of the art. *Eur. J. Pharm. Biopharm.* (2000) Jul; 50(1):161-177.

6. Not only does the art describe various release rates for various drugs in various combinations, the above-cited documents also describe factors that can be controlled in predictable ways to accelerate or decelerate the release of any particular drug, such as a lipophilic drug, a hydrophilic drug, a charged drug or a neutral drug. For example, the rate of release of a lipophilic drug can be decelerated by employing phospholipids with longer acyl chains and can be controlled by adjusting the pH of the internal solution.

7. While the Examiner acknowledges that there is significant skill in the state of the prior art for controlling drug release of single drugs from drug delivery vehicles, he asserts in the November 15, 2007 Office Action that the state of the prior art is not high in terms of "...releasing the two neoplastic agents in the same non-antagonistic ratios." Actually the amount of knowledge of this subject was high at the time of the invention, but experiments were not

reported in the prior art until the present invention, since the knowledge that *ratios* are important AND must be maintained *in vivo* was never appreciated in the art. Therefore the known methods of controlling drug release were never applied to coordinating the release of drug combinations even though practitioners knew how to do it. Once the desirability of controlling ratios was revealed as a result of the present invention, those of skill in the art are able to use the abundant references available to construct delivery vehicles with matched release kinetics of two active agents thereby controlling their ratio after *in vivo* administration.

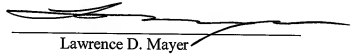
8. For drugs with dissimilar characteristics in which a single delivery vehicle coordinating release of the two drugs is not ideal as described in the specification (paragraphs 0023-0024, 0115, 0117 and 0130), two different carriers modulating the release kinetics of each drug individually can be designed to coordinate the ratio in the blood as demonstrated in Examples 8, 12, and 15 in the specification. The two drug-containing delivery vehicles can be mixed and co-administered *in vivo*. Thus, for example, a combination of a negatively charged drug with a positively charged one might be handled in this way. Coordinated release both from co-encapsulated drugs and drugs formulated separately is illustrated in Examples 8-9, 12-13 and 15-16.

9. Given the breadth of methods available in the prior art for controlling drug release, there are multiple features of each delivery vehicle which could be readily designed to achieve the coordinated release of two encapsulated agents whether co-encapsulated or encapsulated in separate delivery vehicles such that a desired synergistic ratio is maintained in the blood. This could be achieved without undue experimentation based on the extensive data-

base on actual drug release rates from drug delivery vehicles available in the literature for a wide range of drug classes and delivery vehicles.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at Vancouver, CANADA, on January 14, 2008



Lawrence D. Mayer

Curriculum Vitae

DR. LAWRENCE D. MAYER

EXHIBIT A

EDUCATION

Ph.D. Biochemistry (1983) University of Minnesota, Dr. Gary L. Nelsestuen, Supervisor
Thesis: Protein-Membrane Interactions Involved in the Prothrombinase System

B.Sc. Majors in both Chemistry and Biology (1978, *Summa Cum Laude*) Wartburg College

PROFESSIONAL EMPLOYMENT

2003-Present **Founder, President and Head of Research, Celator Pharmaceuticals**

1999-2002 **Founder, President and Chief Executive Officer, Celator Pharmaceuticals**

2004-Present **Adjunct Scientist, BC Cancer Agency**

1992-Present **Adjunct Professor, Faculty of Pharmaceutical Sciences, University of B.C.**

1992-2003 **Senior Research Scientist, Division of Medical Oncology, B.C. Cancer Agency**
Research programs in the development of liposomal drug delivery systems, multidrug resistance and novel chemotherapeutic agents. Graduated 7 Ph.D. students, 3 M.Sc. students and supervised 16 postdoctoral fellows. Awarded over $4M in research funding.

1999-2001 **Research Supervisor, Experimental Medicine, University of B.C.**

1992-2002 **Director, Investigational Drug Program, B.C. Cancer Agency**
Established and directored translational research and development activities of the Investigational Drug Program including GMP production of clinical supplies in the BCCA clean room facility and GLP testing. Co-ordinated proposals for preclinical and clinical testing of new anticancer agents for outside companies as well as development programs for agents generated within the Agency.

1990-1992 **Program Director, QLT Inc.**
Project manager for topical photosensitizer development program. Responsible for implementation of Quality Management system to ensure compliance with HPB and FDA regulatory requirements. Also responsible for directing formulation efforts of topical photosensitizers, coordinating activities between various departments (toxicology, pharmacology, clinical, *etc.*), preparing budget estimates and project administration. Member of Development Management Group responsible for establishing short term and long term corporate drug development strategy.

1987-1990 **Scientific Director, The Canadian Liposome Co. Ltd.**
Project leader of lead liposomal anticancer agent (TLC D-99) at CLC and its parent company The Liposome Co., Inc. (Princeton, N.J.). Responsible for coordinating R&D activities with current time tables for ongoing clinical trials and anticipated production requirements for future trials. Participated in preparing IND submissions to US FDA and Canadian HPB for clinical testing of TLC D-99. Co-directed research projects concerning the mechanism of action of liposomal anticancer pharmaceuticals. Responsible for developing budget requirements for active research projects.

1986-1987 **Research Associate, Biochemistry Dept., University of B.C.**

1983-1986 **Canadian MRC Postdoctoral Fellow, Biochemistry Department, University of B.C.**

AREAS OF SPECIAL INTEREST AND ACCOMPLISHMENTS

- Spearheaded the translation of Celator's CombiPlex fixed-drug ratio combination chemotherapy technology from the lab into the clinic, resulting in two products being evaluated in clinical trials.
- Part of Celator Senior Management team responsible for securing $10MCDN Series A and $40MUS Series B Venture Capital Financings
- Established new paradigm for developing drug combinations for cancer chemotherapy where synergistic drug:drug ratios are fixed inside liposomes for delivery to tumors. This allows drug combinations to be developed based on maximum efficacy rather than on tolerability.
- Co-founder of Celator Technologies as a spin-off of BCCA laboratory focussed on delivery of drug combinations
- Identified novel applications for and characterized the molecular and therapeutic activities of Bcl-2 antisense oligonucleotides used to chemosensitize human solid tumor xenografts which were implemented by Genta, the company developing Genesense.
- Established novel liposome delivery platform based on reactive, cholesterol-free membranes for enhanced disease site-selective activity.
- Identified enhanced lung cancer antitumor activity of vinca alkaloid derivative anhydrovinblastine and led translational research activities that resulted in IND submission for Phase I clinical testing.
- Discovered and characterized use of liposomal anticancer drug formulations in combination with P-glycoprotein inhibitors to effectively treat multidrug resistant tumors, an approach that was validated in later clinical trials.
- Led discovery and translational research activities to develop an optimized liposomal vincristine formulation and led preparation of the IND submission.
- Played leading role in basic and applied research for development of liposomal doxorubicin formulation currently approved for market use in Europe.
- Established and directed operations of the Investigational Drug Program at the BC Cancer Agency. This Program has been granted an Establishment License by the Canadian TPP as a GMP manufacturing clean room and testing facility for clinical trial supplies. This is the only academic center in Canada to hold such accreditation.

HONOURS AND AWARDS

- Nomination in the Ernst & Young Entrepreneur of the Year awards program, in recognition of determination and inspiration in building a thriving business – and a strong and vibrant country (2003)
- Canadian Medical Research Council Postdoctoral Fellow (1983-1986)
- Dissertation Fellowship, University of Minnesota (1982)
- Wayne Page Memorial Outstanding Student-Athlete Award, Wartburg College (1977)

TEACHING

Areas of special interest and accomplishments

- Worked on course coordination committee to develop Cancer Biology graduate course (Path 500)
- Active yearly participation in training of undergraduate students through summer research programs with Faculty of Pharmaceutical Sciences, Pharmacology Dept. and Biochemistry Dept. at UBC

Courses Taught at UBC

Session	Course Number	Scheduled Hours	Class Size	Hours Taught			
				Lectures	Tutorials	Labs	Other
1996-1997	MedGen 421		150	4			
1996-1997	Path 531		17	4			
1997-1998	MedGen 421		150	4			
1997-1998	Path 531		13	4			
1997-1998	Path 548		7	3			
1998-1999	MedGen 421		150	4			
1999	Phar 414				40		
1999-2000	Phar 510		12	8			
2001	Phar 550		50	4			
2001	Phar 414				30		

Graduate students supervised: 7

Students co-supervised: 3

Member of supervisory committees: 12

Postdoctoral fellows supervised: 17

SUMMARY OF GRANTS & CONTRACTS

Total # of grants/contracts held: 29
Range of years: 1992 -- 2006
Total amount of grant money: $9,345,248

INVITED PRESENTATIONS

- "Association of prothrombin, Factor X and Factor V with phospholipid monolayers" FASEB meetings, Chicago, Illinois, May 1982.
- "Protein-membrane interactions involved in the prothrombinase system" Biomembranes Discussion Group, University of British Columbia, December 1982.

- "Influence of transmembrane ion gradients on the transbilayer distribution of dibucaine" Pharmacology Seminar Series, University of British Columbia, October 1985.
- "Optimization of the therapeutic activity of liposomal doxorubicin" FASEB Liposomal Drug Delivery Conference, Saxton, Vermont, July 1987.
- "Liposomal anticancer formulations with improved therapeutic potential" Oncology Experimental Therapeutics Seminar Series, Roswell Park Memorial Institute, Buffalo, New York, March 1990.
- "Development of liposomal vincristine preparations with improved therapeutic potential" Advanced Therapeutics Seminar Series, British Columbia Cancer Agency, Vancouver, B.C., October 1990.
- "Liposomes as intravenous drug delivery systems" Canadian Society of Hospital Pharmacists Annual General Meeting, Vancouver, B.C., November 1990.
- "Pharmacodynamics of liposomal anticancer agents" University of British Columbia, Faculty of Pharmaceutical Sciences Invited Lecture Series, Vancouver, B.C., March 1994.
- "Formulation, toxicity and pharmacology of liposomal doxorubicin" Liposome Research Days Conference, Vancouver, B.C., June 1994.
- "Pharmacology of vincristine encapsulated in sphingomyelin-cholesterol liposomes" AACR Annual General Meeting Discussion Session, Toronto, Ontario, March 1995.
- "Cellular pharmacology of verapamil in P388-ADR cells in vitro" AACR Annual General Meeting Discussion Session, Toronto, Ontario, March 1995.
- "Preclinical and clinical studies with liposomal vincristine" Third Drug Delivery Symposium, Shizuoka, Japan, June 1995.
- "Membrane Properties Control the Therapeutic Activity of Liposomal Vincristine" Fourth Liposomal Research Conference, Freiburg, Germany, August 1995.
- "The Use of Liposomes to Target Anticancer Agents to Solid Tumors" Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, CA, February 1996.
- "Strategies for Optimizing Liposomal Anticancer Agents" PharmTech Conference, East Rutherford, N.J., September 1996.
- "The Use of Liposomes in Therapeutic and Mechanistic Studies of Multidrug Resistance" Canadian Multidrug Resistance Roundtable Meeting, Toronto, Ont., March 1997.
- "Current Trends in Cancer Chemotherapy" Bridging the Strait of Georgia Cancer Research Symposium, Sidney, B.C., May 1997.
- "Therapeutic and Mechanistic Studies on the Pharmacology of Multidrug Resistance" Univ. of British Columbia Dept. of Surgery Seminar Series, Vancouver, B.C., July 1997.
- "In Vivo Entrapment of Doxorubicin Utilising pH Gradient Liposomes" Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, CA, February 1998.
- Strategic Development of Biopharmaceuticals" Pictet Biotechnology Seminar, Vancouver, B.C., September 1998.
- "Designing Liposomal Anticancer Agents to Overcome MDR in Combination with the P-glycoprotein Inhibitor PSC 833" International Conference of Anticancer Research, Thessaloniki, Greece, October, 1998.
- "Optimization of Liposomal Anticancer Drug Formulations for Specific Therapeutic Applications" University of London Liposomes in Biomedical Applications Symposium, London, UK, Dec. 1999.
- "Therapeutic and Pharmacokinetic Properties of Doxorubicin combined with Bcl-2 Antisense Oligonucleotide Treatment" Poster Discussion Session, AACR Annual Meeting, San Francisco, CA, April 2000.
- "Matching Drug Release Kinetics with Therapeutic Applications for Liposomal Anticancer Drug Formulations" International Liposome Research Society Conference, Napa, CA, April 2000.
- "Characterization of a Novel Thermosensitive Liposomal Doxorubicin Formulation for Tumor Specific Drug Exposure" Congress of International Society of Hyperthermia Oncology, Taegu, Korea, April 2000.

- "Application of Liposomal Drug Delivery Systems for Treating Multidrug Resistant Tumors" Pharmacology 2001, Vancouver, BC, March 2001.

CONFERENCE PARTICIPATION (ORGANIZER, KEYNOTE SPEAKER, ETC.)

- Session Chair, "Drug Delivery and Tumor Vascular Targeting" Amer. Assoc. Cancer Res. General Meeting, Philadelphia, PA, April 13, 1999.
- Session Chair, "Gene Targeting" Bridging the Strait of Georgia Cancer Symposium, Vancouver Island, 1998,
- Organizer, Bridging the Strait of Georgia Cancer Symposium, Vancouver Island, 1996 and 1998.
- Session Chair, "Developments in Antisense Technologies", Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, CA, February, 1996.
- Session Chair, "Steric Stabilisation", Fourth Liposomal Research Conference, Freiburg, Germany, August 1995.

MEMBERSHIPS ON SCHOLARLY SOCIETIES, INCLUDING OFFICES HELD AND DATES

- 2005-present: Editorial Academy of the *International Journal of Oncology* (invited)
- 2003-present: American Association for the Advancement of Science
- 1997-present: International Liposome Society
- 1994-present: Parenteral Drug Association
- 1992-present: American Association of Cancer Research
- 1992-present: American Association of Pharmaceutical Sciences
- 1994-present: B.C. Biotechnology Alliance
- 1989-1993: Stanley Park Zoological Society (Elected member of Board of Directors)
- 1992-1994: Biopharmaceutical Innovation Resource Centre/Economic Regional Diversification Agreement Steering Committee

EDITORSHIPS

- 2001-Present: Journal of Experimental Therapeutics and Oncology
- 2001-Present: Molecular Cancer Therapeutics
- 1999-present: International Journal of Oncology

JOURNAL REVIEWER

- 2007-Present European Journal of Pharmaceutical Biopharmaceutics
- 2001-Present Molecular Cancer Therapeutics
- 2001-Present Journal of Pharmaceutical Research
- 1999-Present International Journal of Oncology
- 1998-Present Journal of Pharmaceutical Sciences
- 1998-Present: Cytometry
- 1997-Present Clinical Cancer Research
- 1996-Present: Molecular Pharmacology

- 1996-Present: European Journal of Pharmaceutical Science
- 1996-Present: Journal of Pharmacology and Experimental Therapeutics
- 1995-Present: International Journal of Cancer
- 1994-Present: European Journal of Cancer
- 1993-Present Journal of Liposome Research
- 1992-Present: Journal of the American Chemical Society
- 1991-Present: Cancer Chemotherapy and Pharmacology
- 1991-Present: British Journal of Cancer
- 1990-Present: Journal of Biological Chemistry
- 1990-Present: Cancer Research
- 1987-Present: Biochemistry
- 1987-Present: Biochimica et Biophysica Acta

GRANTING AGENCY REVIEWER

- 2000-2004: Medical Research Council of Canada, Pharmaceutical Sciences Panel
- 1999-2004: Canadian Breast Cancer Research Foundation
- 1997, 1998, 2000: Alberta Cancer Board (External Reviewer)
- 1995-2001: National Cancer Institute of Canada, Panel G, Pharmacology,
- 1995, 1997, 1998: Medical Research Council of Canada (Pharmaceutics Panel, Cancer B Panel)
- 1995-1996: National Cancer Institute of Canada, Panel J

CONSULTANT (ORGANIZATION AND DATES)

- Photovision Pharmaceuticals, Inc., Jenkintwon, PA 2000-2001
- Duke University Hyperthermia Program (M. Dewhirst, Chair), Durham, N.C. 1998-2002
- Elan Pharmaceuticals, Inc., Ireland 1998-1999
- IGT Pharma, Inc., Vancouver, B.C. 1997-2001
- Angiogenesis Technologies, Vancouver B.C. 1995-1997
- QLT Phototherapeutics, Vancouver, B.C. 1993-2000
- Inex Pharmaceuticals, Corp., Burnaby, B.C. 1993-1999

EXTERNAL EXAMINER

- University of Sydney (Pharmaceutical Sciences) June, 2000
- Simon Fraser University (Biology Department) July, 1998

OTHER SERVICE TO THE COMMUNITY

Guest Science Lectures at Mulgrave School, 1997, 1998, 2000
Mulgrave School (North Vancouver) Planning Committee, 1996-1997

PUBLICATIONS

Journals/Refereed

1. **Mayer LD** and Nelsestuen GL (1981) "Calcium and Prothrombin-Induced Lateral Phase Separation in Membranes" Biochemistry 20, 2457-2463.

2. Pusey ML, **Mayer LD**, Wei GJ, Bloomfield VA and Nelsestuen GL (1982) "Kinetic and Hydrodynamic Analysis of Blood Clotting Factor V-Membrane Binding" Biochemistry 21, 5262-5269.

3. **Mayer LD** and Nelsestuen GL (1983) "Membrane Lateral Phase Separation Induced by Proteins of the Prothrombinase Complex" Biochim Biophys Acta. 734, 48-53.

4. **Mayer LD**, Nelsestuen GL and Brockman HL (1983) "Prothrombin Association with Phospholipid Monolayers" Biochemistry, 22, 316-321.

5. **Mayer LD**, Pusey ML, Griep MA and Nelsestuen GL (1983) "Association of Blood Coagulation Factors V and X with Phospholipid Monolayers" Biochemistry, 22, 6266-6233.

6. Nayar R, **Mayer LD**, Hope MJ and Cullis PR (1984) "Phosphatidic Acid as a Calcium Ionophore in Large Unilamellar Vesicle Systems" Biochim Biophys Acta. 777, 343-346.

7. **Mayer LD**, Bally MB, Hope MJ and Cullis PR (1985) "Uptake of Dibucaine into Large Unilamellar Vesicles in Response to a Membrane Potential" J. Biol. Chem. 260, 802-808.

8. **Mayer LD**, Bally MB, Hope MJ and Cullis PR (1985) "Uptake of Antineoplastic Agents into Large Unilamellar Vesicles in Response to a Membrane Potential" Biochim Biophys Acta. 816, 294-302.

9. **Mayer LD**, Hope MJ, Cullis PR and Janoff AS (1985) "Solute Distributions and Trapping Efficiencies Observed in Freeze-thawed Multilamellar Vesicles" Biochim Biophys Acta, 817:193-196.

10. Richards RL, Habbersett RC, Scher I, Janoff AS, Schieren HP, **Mayer LD**, Cullis PR and Alving CR (1986) "Influence of Vesicle Size on Complement-Dependent Immune Damage to Liposomes" Biochim Biophys Acta. 855:223-230.

11. **Mayer LD**, Bally MB and Cullis PR (1986) "Uptake of Adriamycin into Large Unilamellar Vesicles in Response to a pH Gradient" Biochim Biophys Acta. 857:123-126.

12. **Mayer LD**, Hope MJ and Cullis PR (1986) "Vesicles of Variable Sizes Produced by a Rapid Extrusion Procedure" Biochim Biophys Acta 858:161-168.

13. **Mayer LD**, Bally MB, Hope MJ and Cullis PR (1986) "Techniques for Encapsu-lating Bioactive Agents into Liposomes" Chem. Phys. Lipids 40, 333-345.

14. Hope MJ, Bally MB, **Mayer LD**, Janoff AS and Cullis PR (1986) "Generation of Multilamellar and Unilamellar Phospholipid Vesicles" Chem. Phys. Lipids 40, 89-107.

15. Wong KF, Parmar YI, **Mayer LD**, Pritchard PH and Cullis PR (1987) "Detection of Protein-free Lipoprotein Analogues with an Apolar Lipid Core by Freeze-etch Electron Microscopy" Biochim Biophys Acta. 921:411-414.

16. Brenner DE, Arakali AV, **Mayer LD**, Ginsberg RS and Kanter P (1988) "Comparison of Liposomal Doxorubicin and Free Doxorubicin Pharmacokinetics in Rabbit" Clin. Pharmacol. Therapeut. 43, 125.

17. **Mayer LD**, Wong KF, Menon K, Chong C, Harrigan PR and Cullis PR (1988) "Influence of Ion Gradients on the Transbilayer Distribution of Dibucaine in Large Unilamellar Vesicles" Biochemistry 27, 2053-2060.

18. Bally MB, **Mayer LD**, Loughrey H, Redelmeier T, Madden TD, Wong K, Harrigan PR, Hope MJ and Cullis PR (1988) "Dopamine Accumulation in Large Unilamellar Vesicle Systems Induced by Transmembrane Ion Gradients" Chem. Phys. Lipids 47, 97-107.

19. Janoff AS, Kurtz CL, Jablonski RL, Minchey SR, Boni LT, Gruner SM, Cullis PR, **Mayer LD** and Hope MJ (1988) "Characterization of Cholesterol Hemisuccinate and Alpha Tocopherol Hemisuccinate Vesicles" Biochim Biophys Acta. 941:165-175.

20. Balazsovits JAE, **Mayer LD**, Bally MB, Cullis PR, Ginsberg RS and Falk RE (1989) "Analysis of the Effect of Liposome Encapsulation on the Vesicant Properties, Acute and Cardiac Toxicities, and Antitumour Efficacy of Doxorubicin" Cancer Chemother. Pharmacol. 23, 81-86.

21. Redelmeier TE, **Mayer LD**, Wong KF, Bally MB and Cullis PR (1989) "Proton Transport in Large Unilamellar Vesicles in Response to Electrical Potentials and Ph Gradients" Biophys. J. 56, 385-393.

22. **Mayer LD**, Tai LCL, Ko DSC, Masin D, Ginsberg RS, Cullis PR and Bally MB (1989) "Influence of Vesicle Size, Lipid Composition and Drug-to-Lipid Ratio on the Biological Activity of Liposomal Doxorubicin" Cancer Research 49, 5922-5930.

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